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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

CEPERLEY, MARY

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1641

DATE MAILED: 04/02/2004

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/005,050

Applicant(s)

HAUGLAND ET AL.

Examiner

Mary (Molly) E. Ceperley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-70 is/are pending in the application.
- 4a) Of the above claim(s) 57-70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-56 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>4.5</u> . | 6) <input type="checkbox"/> Other: ____. |

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1) Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-56, drawn to methods of fluorescently labeling and detecting immobilized polyamino acids, classified in class 530, subclass 409; class 436, subclass 546; class 435, subclasses 7.5 and 7.9.
- II. Claims 57-70, drawn to kits comprised of a functionalized dipyrrometheneboron difluoride dye in combination with a labeled specific binding pair member, classified in class 530, subclass 391.3; class 436, subclass 808.

2) The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the method of labeling poly(amino acids) of claim 1 (Invention I), which is directed to the reaction between an immobilized poly(amino acid) and a functionalized dye, does not require the use of the kit of claim 57 (Invention II) which is comprised of the combination of a labeled specific binding pair member and a functionalized dye. Further, the two inventions involve different patentability considerations. A patentability determination for Invention I would involve the determination of the novelty and unobviousness of a combination of process steps including a separation of poly(amino acids) by gel electrophoresis, immobilization of the separated poly(amino acids) followed by covalent bonding of the poly(amino acids) to a functionalized dye. A patentability determination for Invention II, on the other hand, would involve the determination of the novelty and unobviousness of the combination of functionalized dye and labeled specific binding pair member independent of any particular method of use of the combination.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter requiring different fields of search and different patentability considerations, restriction for examination purposes as indicated is proper.

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3) During a telephone conversation with Koren Anderson on February 26, 2004 a provisional election was made with traverse to prosecute the invention of Invention I, claims 1-56. Affirmation of this election must be made by applicant in replying to this Office action. Claims 57-70 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4) Applicants are reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5) Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

6) The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7) Claims 1-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) In claim 1, page 56, lines 18-22, the meaning of the bracketed words is unclear.

b) In claim 1, it is unclear whether the term "such that the dipyrrometheneboron difluoride dye has an absorption maximum between 495 nm and 640 nm" is meant to indicate

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that all of the recited dyes have an absorption maximum in the stated range or whether only a subset of the recited dyes has an absorption maximum in the stated range.

c) In claim 1, step d., it is unclear what functional moiety/moieties on the poly(amino acids) are involved in the formation of "a covalent bond" with the "reactive group" of the dye.

d) In claim 4, the plural term "materials" that are poly(vinylidene difluoride)" is inconsistent with the fact that "poly(vinylidene difluoride)" is a single chemical entity.

e) In claim 5, it is unclear whether the combined molecular weight of all the poly(amino acids) is 500 to 200,000 Daltons or whether each poly(amino acid) has the stated molecular weight. See also, claim 34.

f) For claim 11, there is no antecedent basis in claim 9 for the term "the combined labeling mixture".

g) In claim 46, the word --of-- should appear after "capable".

8) The "Background of the Invention" section of the instant specification (see also, the prior art cited on form PTO-1449) establishes that the analysis of poly(amino acids) using a process which involves the combined steps of **i)** separating complex mixtures of poly(amino acids) by gel electrophoresis, **ii)** subsequent electroblotting of the separated protein bands, followed by **iii)** fluorescent counterstaining is a well known technique in the art of protein analysis. See in particular, page 1, line 20 through page 3, line 13 of the instant specification. However, problems associated with the general method are also well established (see page 3, line 15 through page 4, line 16 of the instant specification). The use of the particular dipyrrometheneboron difluoride dyes of the instant invention has been shown to have unexpected advantages in the claimed method (process involving the combination of steps **i)**, **ii)** and **iii)** as described above. See page 5, lines 14-31 of the instant specification and also Table 3 and Example 28.

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9) The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10) Claims 9-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over the admitted prior art as set forth at pages 1 through 5 of the instant specification.

The subject matter of claims 9-56 is directed to the fluorescent labeling of immobilized poly(amino acids) by the covalent attachment of well known dipyrromethene^{boron} difluoride dyes and the subsequent detection of the label.

As described in the instant specification, the technique of covalently labeling poly(amino acids) with fluorescent dyes followed by detecting of a fluorescent optical response is well known in the art. The poly(amino acids) can be immobilized on conventional supports as well as being attached to immobilized aptamers (page 1, line 20 – page 2, line 7).

Given the fact that the dipyrromethene^{boron} difluoride compounds of the instant claims are admittedly well known fluorescent dyes which are useful to label proteins {poly(amino acids)}, it would be obvious to substitute these dyes as equivalents for the fluorescent dyes used in the prior art processes of labeling immobilized poly(amino acids), as claimed, with the expectation of obtaining a similarly useful labeling process with the known advantages accruing to the use of dipyrromethene^{boron} difluorides. See in particular, the specification, page 4, line 28 – page 5, line 10 for a discussion of the desirable features of the dipyrromethene^{boron} difluoride dyes of the instant claims and page 14 of Haugland, Handbook of Fluorescent Probes and Research Chemicals, 6th edition (cited on form PTO-1449) for a discussion of the use of these dyes to label peptides {poly(amino acids)}.

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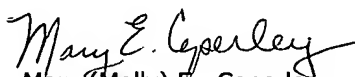
The features of the dependent claims are either specifically described by the references or constitute obvious variations in parameters which are routinely modified in the art (e.g. conventional concentrations of dyes of claim 11; time of illumination of labeled poly(amino acids) of claim 36) and which have not been described as critical to the practice of the invention. For example, for the use of a dipyrromethene^{brown} difluoride succinimidyl ester of a carboxylic acid as recited in claim 10, see page 14 of Haugland, Handbook of Fluorescent Probes and Research Chemicals, 6th edition, "BODIPY Succinimidyl Esters" (cited on form PTO-1449).

11) An inquiry of a general nature which is **not related to the prosecution on the merits** should be directed to Technology Center 1600 telephone number (571) 272-1600. The general fax number for the USPTO is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (571) 272-0813. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (571) 272-0823.

March 30, 2004


Mary (Molly) E. Ceperley
Primary Examiner
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